Clinicopathological Study of Acute Leukemia - A Multiparameter Study

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ABSTRACT

Introduction: Acute leukaemia is major group of haematological malignancies which need timely diagnosis and initiation of treatment at time because in initial stage of disease leukemic cell burden is low. Therefore the chances of achieving complete remission will be highest. Detection of immature leukemic cells in peripheral smear along with presence of clinical signs and symptoms are most important clue for timely diagnosis. The objectives of the present study were to determine the frequency of presenting clinical sign and symptoms and correlate them with laboratory data, morphological features of leukemia and prognostic factors in leukemia patients.

Material and Methods: The present study (2014) was done in the haematology, a section of central pathology laboratory, Department of Pathology of Gajra Raja Medical College, Gwalior over a period of one year from 1st October 2013 to 30th September 2014. This was a prospective study of one year duration. The blood samples of suspected cases of leukemia were received from all departments of Jayarogya hospital particularly from the paediatric and medicine departments.

Results: Out of the 83 cases diagnosed as acute leukaemia, 46 (55.4%) were AML and 37 (44.6%) were ALL. 53 cases (63.85%) were male whereas 30 cases (36.15%) were female. Male-female ratio was 1.76:1. Highest number of cases which comprising 25.3% (83/21) of total cases belonged to 11-20 years of age group followed by 20.28% and 19.27% belonged to 21-30 years and 0-10 years of age group respectively. AML M2 FAB subtype which comprising 39.13% cases of all AML cases was most common FAB subtype followed by AML M1 (19.56%) and AML M4 (17.39%) whereas ALL L1 FAB subtype was more common as compare to FAB L2 subtype.

Conclusion: In our study (2014), AML was more common as compared to ALL and acute leukaemia was more prevalent in males than in females and ALL was common in childhood as compared to AML which is more common in adults. AML M2 and ALL L1 FAB subtype was more common in their respective group.

Keywords: Acute Leukaemia, ALL, AML, symptoms, anaemia, Leukocytosis.

INTRODUCTION

Leukemia is a group of hematological malignancy in which there is unregulated and rapid proliferation of leukemic cells results in replacements of normal hematopoietic precursor cells of erythroid, megakaryocytic, myeloid or lymphoid lineage by proliferating leukemic cells in bone marrow. This manifests in form of anemia and/or thrombocytopenia with leukocytosis or in form of pancytopenia with presence of immature leukocytes in peripheral blood. When blasts cells are more than 20% in bone marrow and/or peripheral blood, the leukemia is designated as acute leukemia. If not treated, acute leukemia results in death within a few weeks or within month. Therefore it is important that leukemia must be diagnosed as soon as possible so that the treatment can be started in early stage of disease when leukemic burden is low. A number of recurrent genetic abnormalities play an important role in malignant transformation of leukemic cells. The objectives of the present study were to determine the frequency of presenting clinical sign and symptoms and correlate them with laboratory data, morphological features of leukemia and prognostic factors in leukemia patients.

MATERIAL AND METHODS

The present study (2014) was done in the haematology, a section of central pathology raboratory, Department of Pathology of Gajra Raja Medical College, Gwalior over a period of one year from 1st October 2013 to 30th September 2014. This was a prospective study of one year duration. The blood samples of suspected cases of leukemia patients were received from all departments of Jayarogya hospital particularly from the paediatric and medicine departments.

Of all the bone marrow samples received in hematology section, 83 cases were diagnosed as acute leukemia. The clinical history and other data of all acute leukemia patients were collected. Their EDTA-anti coagulated blood was used for CBC and peripheral smear examination. CBC was performed on fully automated five part differential cell counter (Mindray-BC 5380). Wherever required improved Neubauer's chamber and Wintrobe's hematocrit tube were used for blood cells counting and packed cell volume measurement respectively.

The peripheral smears and bone marrow aspiration were stained by Leishman's stain and examined using oil immersion lens. Acute leukemia cases were diagnosed by the morphology of leukemic cells (immature cells of myeloid or lymphoid series) and presence of such leukemic cells more than 20% in peripheral blood and or bone marrow, and were further classified in AML and ALL on the basis of their morphologic features. Sometimes it is very difficult to classify acute leukemia in myeloid and lymphoid lineage accurately. In such cases modern modalities like flowcytometry, cytochemistry, cytogenetics and molecular study are required to classify the cases of acute leukemia in myeloid and lymphoid Lineage. In developing country like India the new modalities, flowcytometry and cytochemistry are not available in most of the laboratories and in our center too.

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STATISTICAL ANALYSIS

Descriptive statistics like mean and percentages were used to interpret the results. Microsoft office 2007 was used to make tables.

RESULTS

During the twelve months period of our study from October 2013 to October 2014, 83 blood and bone marrow aspirate samples from acute leukemic cases were studied in the Department of Pathology, Gajra Raja Medical College and J.A. Group of Hospitals, Gwalior. Out of total 83 cases (100%) of acute leukemia, 46 cases (55.4%) were AML and 37 cases (44.6%) were ALL. The observations are as follows:

In present study (2014) total 83 cases (100%) of acute leukemia were studied, 53 cases (63.85%) were male and 30 cases (36.15%) were female. Male –female ratio was 1.76:1. Out of 83 cases of acute leukemia, 46 cases (55.4%) were Acute Myeloid Leukemia (AML) and 37 cases (44.6%) were Acute Lymphoblastic Leukemia (ALL). Amongst AML group, 28 patients were males (60.86%) and 18 patients were females (39.14%) while in ALL group 25 cases (67.57%) were male and 12 cases (32.43%) were female.

In present study (2014) the age wise distribution revealed that 16 cases(19.27%) belonged to 0-10 years of age group followed by 21 cases (25.3%) which comprising highest number of

cases belonged to 11-20 years of age group, 17 cases (20.28%) belonged to 21-30 years of age group, 14 cases (16.86%) belonged to 41-50 and 13 cases (15.66%) belonged to 51-60 years of age group while only 03 cases (3.61%) were of 51-60 years of age group, 02 cases (2.4%) were of 51-60 years of age group and 01 case (1.2%) was of 51-60 years of age group.

In present study (2014) the age wise distribution showed that ALL is more common in children whereas AML is more common in adult age group.

Present study (2014) showed the distribution of leukaemia patients according to FAB sub-types of AML and ALL. In AML group out of total 46 cases(100%), 1 case (2.17%) belonged to AML M0 FAB subtype, 09 cases (19.56%) belonged to AML M1 subtype, 18 cases (39.13%) belonged to AML M2 subtype which comprises highest number of cases, 4 cases (8.69%) belonged to AML M3 subtype, 08 cases (17.39%) belonged to AML M4 subtype, 05 cases (10.86%) belonged to AML M5 subtype and 01 case (2.17%) belonged to AML M6 subtype. NO case was found of AML M7 subtype while in ALL group out of total 37 cases (100%), 21 cases (56.75%) showed FAB ALL L1 subtype and 16 cases (43.25%) were found of FAB ALL L2 subtype. No case of FAB L3 ALL subtype was found.

Table-2 shows the laboratory indices in AML group, out of total 43 cases (100%), 1 case showed leucopenia (total count< 4000/cumm), 3 cases (6.51%) had leucocyte count within normal range (4000-11,000/cumm), 7 cases (15.21%) had leucocyte count between 11,000-50,000/cumm. 14 cases (30.43%) showed 50,000-100,000/cumm, maximum 16 cases (34.78%) fall in the range of 100,000-200,000/cumm and 6 cases (13.04%) showed leucocyte count more then 200,000/cumm.

Anaemia was detected in 100% of AML patients. There was severe degree of anemia in 50% of cases (Hb <6 g/dl), and 39.13% had moderate degree of anaemia (Hb: 6.1-9 g/dl) while 10.87% cases had mild anaemia. No case showed Hb% more than 12gm%.

20 cases of AML (43.47%) showed platelets count between 50,000-1,00,000/cumm, 17 cases (36.95%) showed 20,000-50,000/cumm, while eight cases (17.39%) showed platelets

S. No	Age	AML	ALL	Total	
				No	%
1.	0-10	02	14	16	19.27
2.	11-20	05	16	21	25.3
3.	21-30	10	05	17	20.28
4.	31-40	12	01	14	16.86
5.	41-50	11	01	13	15.66
6.	51-60	03	0	03	3.61
7.	61-70	02	0	02	2.4
8.	71-80	01	0	01	1.2
Total		46	37	83	100

Table-1: Age wise distribution

Parameter	Range	AML		ALL	
		No.	%	No.	%
TOTAL WBC Count/cumm	<4000	01	2.17	4	10.81
	4000-11000	02	4.34	3	8.11
	11100-25000	07	15.21	8	21.62
	25100-50000	14	30.43	6	16.2
	50100-100000	16	34.78	8	21.62
	>100000	06	13.04	8	21.62
Hb (Gm%)	<6	23	50	8	21.62
	6.1-9	18	39.13	24	64.87
	9.1-12	05	10.87	5	13.5
Platelet count / cu mm	<20000	08	17.39	6	16.22
	20000-50000	17	36.95	17	45.95
	50100-100000	20	43.47	12	32.43
	>100000	01	2.17	2	5.4
% of blasts in peripheral blood on first presentation	<20%	-	-	1	2.7
	20-50%	-	-	7	18.91
	51-80%	-	-	21	56.76
	>80%	-	-	8	21.63

Table-2: Frequency of laboratory indices in leukemic patients

S. No.	Symptoms	AML		ALL	
		No.	%	No.	%
1	Fever	40	86.95	31	83.78
2	Generalized weakness	24	52.75	26	70.27
3	Loss of appetite	17	36.95	10	27
4	Loss of weight	09	19.56	6	16.21
5	Pallor	39	84.78	32	86.48
6	Lymphadenopathy	21	45.65	25	67.57
7	Splenomegaly	17	36.95	18	48.65
8	Sternal tenderness	0	0	8	21.62

Table-3: Frequency of clinical symptoms and signs

count less than 20,000/cumm and only one case (2.17%) showed platelets count more than 1,00,000/cumm.

While in ALL group complete blood cell count was found abnormal in all of the patients and pancytopenia was detected in 10.81% of the patients. Of all the ALL patients, 91.89% had abnormal WBC count at presentation, 10.81 had leucopenia and 80% had leukocytosis. WBC count was above 50,000/cumm in 21.62% of cases and 21.62% of patient had WBC count more than 1.0lakh/cumm.

Anaemia was detected in 100% of ALL patients. There was moderate degree of anemia in 64.87% of cases (Hb: 6.1-9 g/dl), and 21.62 had severe anaemia (Hb<6 g/dl) and 13.5% cases had mild anaemia.

Platelet count was more than 1,00,000/cumm in 5.4% of ALL patients, 45.95% had platelet count between 20,000-50,000/cumm, 32.43% patient had platelet count between 50,100-1,00,000 /cumm and 16.22% patient had count below 20,000/cumm.

One case (2.7%) of ALL showed blast cell less than 20%, 7 cases (18.91%) showed blast cells between 20% to 50%, 21 cases (56.76%) showed blast cell between 51% to 80% and 8 cases (21.63) showed blast cells more than 80%.

Table-3 reveales that fever was the commonest clinical symptoms, followed by generalized weakness, loss of appetite and loss of weight while pallor was commonest clinical sign followed by lymphadenopathy, splenomegaly and sterna tenderness.

DISCUSSION

Present study was conducted at department of pathology J.A. Group of hospitals and G.R. Medical College, Gwalior from Oct. 2013 to Oct. 2014 and total 83 cases of acute leukemias had been studied. Acute Leukemias were mainly classified into AML and ALL, on the basis of clinical course of disease, laboratory data and morphological features of leukemic cells. Of total 83 cases (100%) of acute leukemia, 46 cases (55.4%) were AML and 37 cases (44.6%) were ALL.

In present study (2014), it was found that acute leukaemias were more common in male (63.85%) as compared to female(36.15%), male to female ratio was 1.76:1. In ALL, male to female ratio was 2.08:1 and in AML, male to female ratio was 1.55:1. These findings were comparable to the studies conducted by GUPTA RAJAT et al (2015)[3] they reported male to female ratio - 1.94:1, 2.05:1 and 1.82:1 in acute leukemia, ALL and in AML respectively in their study.

Present study (2014) showed that prevalence of AML (55.4%) was higher as compared to that of ALL (44.6%). Similar findings have been reported by Khalid Hassan et al (1993).[6] Studied conducted by Laishram RS et al (2011)[9], Vinsheth et al (2002)[19], and Kulshreshtha R et al (2002)[8] also showed the higher prevalence of AML as compared to that of ALL.

In Present study (2014), AML was more prevalent and 46 cases (62.14%) of AML out of total 83 cases of acute leukemia had been found. Findings of present study (2014) is similar to that reported by Laishram R S et al (2011)[9] as 61.36%.

In present study (2014), on age wise distribution of leukaemia patients it was found that the majority of patient (25.3%) of acute leukaemia were belonged to age group of 11-20 years followed by (20.28%) cases in age group of 21-30 years and (19.27%) cases in age group of 0-10 years. Findings of our study are not exactly comparable to study conducted by GUPTA RAJAT et al (2015).[3] They reported majority of cases (35%) in age group of 0 -10 years, followed by (21%) cases in age group of 11-20 years and (19%) cases in age group of 21-30 years. In both studies (present study and Gupta Rajat et al), it was found that acute leukemia is more common in patients less than 30 years of age.

In present study, the cases of AML and ALL were further classified into morphological subtypes according to the FAB classification. Amongst AML group, we found that AML M2 was the commonest FAB subtype seen in 39.13% of cases followed by M1 (19.56%), M4 (17.39%), M5 (10.86%) and M0 (2.17%) and M6 (2.17%) cases. AML M7 was not found in our study. These findings were comparable to the studies conducted by Dick FR et al(1982)[2,17,7] Horibe K et al (2001)[5], Rego MF et al (2003)[12] and Rodrigues CA et al(2003).[13] Hassan K et al(1994)[6] in their study reported M4 as the commonest subtype of AML followed by M2, M1 M3 and M5 and M6 and M7 respectively. Harani MS et al (2005)[4] also reported M4 as the predominant FAB subtype seen in 36.2% of cases followed by M2 (30.25%), M3 (10.4%), M1 (8.7%), M0 (7.7%), M5a (3.5%), M5b (2.5%) and M6 (0.8%).

Out of 37 cases of ALL, L1 was the commonest subtype seen in 56.75% of cases followed by L2 (43.25%). No case of ALL L3 was found in our study. These findings were comparable to the studies conducted by[6,14] and Van EJ et al (1986).[15] However these findings did not match with those of Dick FR et al (1982)[2] who reported L2 as the commonest subtype seen in 60% cases followed by L1 (31%) and L3 (9%) respectively. Paul B et al (1992)[11] reported L2 morphology in 69% of cases of ALL.

In our study all clinical signs and symptoms of acute leukemia patients had been recorded at the time of first presentation and on analysis of these clinical signs and symptoms, it was found that fever was the most common clinical symptom followed by generalized weakness and loss of appetite while pallor, splenomegaly and hepatomegaly were commonest clinical sign. Lymphadenopathy was more common in ALL as compare to AML. These findings are comparable with the study conducted by Gupta Rajat et al (2015).[3,1,14,10]

CONCLUSION

In our study (2014), AML was more common as compared to ALL and acute leukaemia was more prevalent in males than in females and ALL was common in childhood as compared to AML which is more common in adults. AML M2 and ALL L1 FAB subtype were most common in their respective group.

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